Pathologies sin which mechanics or “mechanobiology” is implicated

- Asthma
- Atherosclerosis
- Cancer
- Arthritis
- Hypertension
- Bone healing
- Loss of bone mass
- Pulmonary fibrosis
- Surfactant release in lung
Expt. #2: Cell Squashing (and AFM)

Scaling solution

\[ F \sim GR^{1/2} \delta^{3/2} \]

Exact solution for a sphere

\[ F = \frac{4ER^{1/2}}{3(1-\nu^2)} \delta^{3/2} \]

From top, a round cell, a spread cell and a nucleus. (Caille, et al., J. Biomech, 2002)

Population averaged force–relaxation curves showed similar trends for both HeLa and MDCK cells, with a rapid decay in the first 0.5 s followed by slower decay afterwards (Fig. 1d(I)). In Fig. 1d(II), we see that force–relaxation clearly exhibited two separate regimes: a plateau lasting ~0.1–0.2 s followed by a transition to a linear regime (Fig. 1d(II)). Hence, at short timescales, cellular force–relaxation does not follow a simple power law. Comparison with force–relaxation curves acquired on physical hydrogels\textsuperscript{22,23}, which exhibit a plateau at short timescales followed by a transition to a second plateau at longer timescales (Supplementary Fig. S3A,B), suggests that the initial plateau observed in cellular force–relaxation may correspond to poroelastic behaviour. Indeed poroelastic
Simple Display System of Mechanical Properties of Cells and Their Dispersion

Yuji Shimizu¹, Takanori Kihara¹, Seyed Mohammad Ali Haghpardast¹, Shunsuke Yuba², Jun Miyake¹

B  
Cell  
BSA coating  
Dish surface  

C  

E = 929.8 Pa  

Force (nN)  
Depth of indentation (µm)  

A  
Spherical probe  

\[ F_v = \frac{4}{3} \delta^3 \left( \frac{E_v}{1 - \nu^2} \right) \frac{R_1 R_2}{R_1 + R_2} \]  

Cell object  

March, 2012

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Homogeneous??

Cells in 3D matrix

MDA-MB-231 breast cancer cells migrating inside a collagen gel.

- Dense cortical actin with myosin.
- Cross-linkers more homogeneously distributed

Rajagopalan, unpublished
Isotropic??

Figure 3 | Sheet-like cell protrusion comprises two layers of actin networks with distinct structures. (a) Dual-objective STORM image of actin in a BSC-1 cell. The z positions are color coded (color bar). (b,c) Vertical cross sections (each 500-nm wide in x or y) of cell in a along dotted and dashed lines, respectively. When far from cell edge, z position of dorsal layer increases quickly and falls out of imaging range. (d,e) The 2 profiles for two points along vertical section (red and yellow arrows in b, respectively). Each histogram is fit to two Gaussians (red curves), yielding apparent thickness of ventral and dorsal layers and peak separation between the two layers. (f) Quantification of apparent thickness averaged over two layers and dorsal-ventral separation obtained from x-z cross-section profile in b. (g,h) Ventral and dorsal actin layers of cell in a. (i,j) Ventral and dorsal actin layers of a COS-7 cell treated with blebbistatin. (k,l) Vertical cross sections (each 500-nm wide in x or y) of cell along dotted and dashed lines, respectively. (m) Actin density of ventral and dorsal layers along yellow box in i,j, measured by localization density. Scale bars, 2 µm (a,g–j); 100 nm for z and 2 µm for x and y (b,c,k,l).

We observed two vertically separated actin layers in the sheet-like cell protrusion despite its small thickness (Fig. 3a–c). The apparent thickness of each layer was

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http://www.nature.com/nmeth/video/moy2008/index.html
Elastic??

Micropipette Aspiration

Cells are viscoelastic

![Graph showing force and indentation depth](image)

Force (0-4.5 nN)

Indentation depth (0-1.6 μm)

**Indentation**

(Zahalak et al., 1990)
Figure 1 removed due to copyright restrictions. 
Background: Linear Rheology of the Cytoskeleton

- Cells exhibit a weak power-law rheology, similar to soft glassy materials.
- This behavior is consistent over a range of experimental conditions and for all different types of cells.

\[ G^* = G' + jG'' = \alpha \frac{M(t)}{\delta(t)} \]

\[ G = G_0 \left( \frac{\omega}{\omega_0} \right)^{x-1} \frac{1 + j\eta}{\pi} \Gamma(x-2) \cos \left[ \frac{\pi}{2} (x-1) \right] + j\omega \mu \]

\[ \eta = \tan(x-1) \frac{\pi}{2} \]
Expt. #4: Cell stretching
Desprat et al., Biophys J., 2005.

Power-law behavior observed over a wide range of strains.

\[ \frac{d\varepsilon}{dt} = \text{const} \cdot t^\alpha. \]

Cells can appear to exhibit simple viscoelastic behavior in a linear plot, but on log-log scales the power-law behavior becomes obvious.

Population averaged force–relaxation curves showed similar trends for both HeLa and MDCK cells, with a rapid decay in the first 0.5 s followed by slower decay afterwards (Fig. 1d(I)). In Fig. 1d(II), we see that force–relaxation clearly exhibited two separate regimes: a plateau lasting \( \sim 0.1–0.2 \) s followed by a transition to a linear regime (Fig. 1d(II)). Hence, at short timescales, cellular force–relaxation does not follow a simple power law. Comparison with force–relaxation curves acquired on physical hydrogels\(^{22,23}\), which exhibit a plateau at short timescales followed by a transition to a second plateau at longer timescales (Supplementary Fig. S3A,B), suggests that the initial plateau observed in cellular force–relaxation may correspond to poroelastic behaviour. Indeed poroelastic
Expt. #5: Particle Tracking Microrheology (PTM)  
(T. Savin)  
• Standard video microscopy tracking setup  

Courtesy of MIT.
Video Microscopy Particle Tracking

- Tracking algorithms

Example:
1 μm diameter spheres in water, $T=25^\circ$C

Crocker and Grier, 1996

http://www.physics.emory.edu/~weeks/idl/
Particle tracking microrheology

• Thermal fluctuations of particles reflect the mechanics of their local environment

• Evaluate the mean-squared displacement of the particles:
\[ \langle \Delta x^2(t) \rangle = \langle |x(t) - x(0)|^2 \rangle \]

• Two limits

  **Viscous**
  \[ \langle \Delta x^2(t) \rangle = \frac{k_B T}{\pi a \mu} t \]

  **Elastic**
  \[ \langle \Delta x^2(t) \rangle = \frac{k_B T}{\pi a G} \]
Particle tracking microrheology

- Generalized Stokes-Einstein Relation (GSER)
  \[
  \hat{G}(\omega) = \frac{k_B T}{\pi a j \omega F_t^u \langle \Delta x^2(t) \rangle} = G'(\omega) + jG''(\omega)
  \]

- Example - Voigt fluid:
  \[
  \hat{G}(\omega) = G + j\mu \omega
  \]

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Tumor cell escaping from the circulation

Figure removed due to copyright restrictions.

Michelle Chen, Integr Biol, 2013
Nonlinear modulus at higher levels of prestress

A prestress is applied to the network and the deformation is measured in response to an additional oscillatory stress.

The response is approximately linear with prestress above a threshold value.

Incremental modulus is independent of actin or cross-link concentration.

Courtesy of the National Academy of Sciences. Used with permission.
Pre-stress increases moduli of reconstituted F-actin networks, up to a critical point

Reconstituted actin gels

Strain-stiffening of F-actin/ABP at low strains
Nonlinear stress response and matrix collapse at large strain
Reversible stress stiffening and softening

(Tseng et. al. 2004)

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(Chaudhuri et al. 2007)

Reconstituted cellular cytoskeletons

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Strain stiffening
Collapse

(Chaudhuri et al. 2007)

Nonlinear stress response and matrix collapse at large strain
Reversible stress stiffening and softening

Neutrophil elastic moduli fall abruptly upon deformation into a capillary

(Yap & Kamm, J Appl Physiol, 2005)
Cells that have been suddenly stretched immediately exhibit a lower G’ but recover in ~ 200s

